UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,621	12/21/2001	Walter Callen	DIVER1350-6	9848

20985 7590 04/28/2004

FISH & RICHARDSON, PC
12390 EL CAMINO REAL
SAN DIEGO, CA 92130-2081

EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/034,621	CALLEN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 28-44* is/are pending in the application.

4a) Of the above claim(s) *34,35, 38 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,28-33,36,37 and 39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *44* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of the specification and amendment canceling claims 18-27, without prejudice, amending claims 1-6, 8-17, 31-33, 37 and the addition of new claims 39-44 in the paper of 1/22/2004, is acknowledged. Claims 1-17 and 28-44 are still at issue and are present for examination.

Election/Restrictions

Newly submitted claim 44 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

VII. Claims 44, drawn a method for producing a biologically active polypeptide and screening the polypeptide for enhanced activity, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Inventions of currently prosecuted Groups I, original claims 1-17 and newly added Group VII (claim 44) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acid of currently prosecuted Group I can be used to mutate or synthesize the encoded polypeptide.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

Accordingly, claim 34, 35, and 38 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 34, 35, 38 and 44 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is indefinite in that it is drawn to an isolated or recombinant nucleic acid encoding a polypeptide having a sequence as set forth in SEQ ID NO: 2 or (b) enzymatically active fragments of (a). It is unclear as to the enzymatic activity to which applicants refer in part (b). It is understood that the polypeptide having the amino acid sequence of SEQ ID NO: 2 has multiple enzymatic activities and thus it is unclear to which one, if not more then one applicants refer.

Related somewhat to the above rejection over claim 16, claim 17 is indefinite in that it is drawn to an isolated or recombinant nucleic acid encoding a polypeptide comprising at least 20 consecutive amino acids of (a) SEQ ID NO: 2 or (b) enzymatically active fragments of (a). It is unclear as to the enzymatic activity to which applicants refer in part (b). While with respect to claim 16, it is understood that the polypeptide having the amino acid sequence of SEQ ID NO: 2 has multiple enzymatic activities and thus it is unclear to which one, if not more then one, applicants refer, claim 17 part (a) merely refers to a nucleic acid which encodes a polypeptide comprising at least 20 consecutive amino acids of SEQ ID NO: 2, and need not necessarily encode a polypeptide with a defined function. Thus more so then claim 16, claim 17 is unclear to which "enzymatic activity" applicants refer.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6, 7-11, 12-17 and 39-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 4-6, 7-11 and 12-17. In response to this rejection applicants have amended claims 4-6, 8-17 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that applicants were in possession of the claimed invention at the time of filing as applicants submit that a single species of a genus can be sufficient to put one of skill in the art in possession of all species within a claimed genus.

Applicants further submit that only structurally and functionally related nucleic acids are encompassed by the scope of the claims as the claimed invention is described by structure (the exemplary sequences), a physico-chemical property and function (polymerase activity). Applicants also refer to example 14 of the USPTO guidelines concerning compliance with written description in supporting applicants position.

Applicants traversal has been considered in full, however applicants traversal is found nonpersuasive because applicants argue that the rejected claims include both structural and functional limitations, however applicants are reminded that the rejected claims have no functional limitations, (i.e. See claims 4-6, 7-11 and 12-17). Thus any argument based on such a functional description of the claimed genus is in error and found nonpersuasive. Claims 39-43 are included in the rejection for the same reasons originally stated for claim 12.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 4-6 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically applicants newly added amendment of the specific hybridization conditions of each of claims 4, 5 and 6 are not supported by the original specification at the time of filing. It is requested that applicants indicate where in the specification applicants have support for the specific hybridization and wash conditions recited in each of claims 4, 5 and 6.

Claims 1-3, 4-6, 7-11, 12-17, 28-33, 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acid comprising SEQ ID NO: 1 and encoding a polypeptide having polymerase activity, does not reasonably provide enablement for any nucleic acid comprising a mere 70% identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity, or any nucleic acid comprising a mere 10 consecutive bases of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1-3, 4-6, 7-11, 12-17, 28-33, 36 and 37. In response to this rejection applicants have amended claims 1-6, 8-17 1-6, 8-17, 31-33, 37 and added new claims 39-43 and traverse the rejection as it applies to the newly amended claims. In support of applicants traversal it is acknowledged that applicants have submitted a declaration of Dr. Jay Short, an inventor of the instant application.

Applicants submit that the specification enabled the skilled artisan at the time of the invention to identify and make and use, a genus of polymerases to practice the claimed invention. Applicants point out, as declared by Dr,. Jay short, one of the inventors of the invention, that the state of the art and the level of the person of ordinary skill in the art was very high and that one of skilled in the art could have used routine methods known in the art at the time of the invention, including those described in the specification, to screen for nucleic acids encoding polypeptides having a percent sequence identity to SEQ ID NO: 1 for various polymerase activities.

Applicants argument and the declaration submitted by Dr. Short have been fully considered, however are found nonpersuasive for the following. First as pointed out to applicants above under the rejection based on a lack of written description, the claimed genus(s) are not limited to those nucleic acids encoding polymerases. Applicants are respectfully reminded that only claims 1-3, 28-33, 36 and 37 are limited to those nucleic acids encoding a polymerase or fragments having the enzymatic activity of a

polymerase. Claims 4-17 are not limited to a genus of nucleic acids which encode a polymerase and thus applicants argument does not apply to claims 4-17.

In response to applicants argument as it applies to claims 1-3, 28-33, 36 and 37, drawn to those nucleic acids which must encode a polymerase, is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a polymerase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the nucleic acid structure which may be modified without effecting the desired activity; (B) the general tolerance of the encompassed nucleic acids to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would

be required to determine which substitutions would be acceptable to retain the desired activity/function and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus defined merely as all nucleic acids comprising a sequence having at least 70% sequence identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity. Claims 39-43 are included in the rejection for the same reasons originally stated for claim 12.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid modifications of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4-6, 7-11, 12-15, 17 and 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand et al. (U.S. Patent No. 5,491,086, issued 2/13/1996).

The rejection was stated in the previous office action as it applied to previous claims 4-6, 7-11 and 12-17. In response to this rejection applicants have amended claims 4-6 and 8-17 and traverse the rejection as it applies to the newly amended claims. For applicants convenience the original rejection is repeated below.

Gelfand et al. teach a purified thermostable nucleic acid polymerase and DNA encoding said polymerase from *Pyrodictium* species. Gelfand specifically teach a nucleic acid from *P. occultum* (SEQ ID NO: 3) which is substantially identical to instantly disclosed SEQ ID NO: 1, as "substantially identical" is defined in the instant disclosure as two or more nucleic acid sequences that have at least 60% nucleotide identity (See page 14, lines 17-24 of specification) and SEQ ID NO: 3 disclosed by Gelfand is 66.5% identical to instantly disclosed SEQ ID NO: 1. Further the DNA taught by Gelfand et al. comprises many regions of at least 10 consecutive bases of sequence as set forth in SEQ ID NO: 1 and encodes a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2.

Thus, Gelfand et al. anticipates claims 12-17 drawn to a recombinant nucleic acid, comprising at least 10 consecutive bases of SEQ ID NO: 1, or encoding a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO: 2. Gelfand et al. further anticipates claims 4-6 drawn to a recombinant nucleic acid that hybridizes to the nucleic acid comprising a sequence having at least 70% identity to SEQ ID NO: 1

and encoding a polymerase (claim 1) under conditions of high to low stringency. Gelfand et al. further anticipates claims 7-11 drawn to a recombinant nucleic acid having at least 70% to 95 % sequence identity to a nucleic acid having at least 70% sequence identity to SEQ ID NO: 1 and encoding a polymerase (claim 1).

Applicants traverse the rejection on the basis that applicants amendment will cause the in the previous rejection of the claims by Gelfand et al. to be withdrawn. Applicants submit that after such an amendment the claims are drawn to nucleic acids hybridizing under specific hybridization conditions, which do not encompass nucleic acids merely 66.5% identical to instantly disclosed SEQ ID NO: 1. Applicants further point out that also after entry the claims are drawn to nucleic acids comprising at least 20 consecutive bases of SEQ ID NO: 1 or 20 consecutive bases of a sequence having at least 70% identity to SEQ ID NO: 1 and encoding a polypeptide having polymerase activity.

Applicants amendment has resulted in the withdrawal of claim 16 from the current rejection.

Applicants argument has been considered in full, however it has been found non persuasive for the reasons previously stated and those below.

First as discussed above under the 112 first paragraph rejections, claims 4-17 are not limited to a genus of nucleic acids which encode a polymerase . Thus all of the rejected claims, 4-6, 7-11 and 12-17are merely drawn to nucleic acids which are described structurally, but lack any functional limitations.

Gelfand et al. anticipates claims 4-6 drawn to a recombinant nucleic acid comprising **a** sequence that hybridizes a nucleic acid having a sequence as set forth in SEQ ID NO: 1 under the specified conditions. Applicants is reminded that the sequence taught by Gelfand et al. comprises many sequences that in and of themselves would hybridize to SEQ ID NO: 1, thus anticipating the claims to "a nucleic acid comprising **a** sequence which hybridizes..." This is in spite of the overall homology of the full length sequence taught by Gelfand et al. and whether or not the full length sequence would hybridize to SEQ ID NO: 1.

Gelfand et al. further anticipates claims 7-11 drawn to a recombinant nucleic acid having at least 70% to 95 % sequence identity to a nucleic acid having at least 70% sequence identity to SEQ ID NO: 1 and encoding a polymerase (claim 1). As a means of further illustrating the reasons the examiner has maintained the rejection of these claims by Gelfand et al. applicant is requested to determine the percent sequence identity to SEQ ID NO: 1 of the genus of nucleic acids claimed in claim 10, taking into consideration that claim 10 is 95% identical to claim 9, which is 90% identical to claim 8, which is 70% identical to SEQ ID NO: 1.

Gelfand et al. anticipates claim 12 drawn to a recombinant nucleic acid, comprising at least 20 consecutive bases of SEQ ID NO: 1 and those nucleic acids at least 70, 80%, or 90% identical to a recombinant nucleic acid, comprising at least 20 consecutive bases of SEQ ID NO: 1 (claims 13-15).

Gelfand et al. anticipates claim 17 drawn to a recombinant nucleic acid, encoding a polypeptide comprising at least 20 consecutive amino acids of SEQ ID NO: 2 .

Newly added claims 39-43 are included in this rejection because Gelfand et al. further teaches methods for making a polypeptide comprising expressing the taught nucleic acids in an expression vector, and prokaryotic and/or yeast host cells

Double Patenting

The rejection of claims 1-17, 28-33, 36 and 37 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of U.S. Patent No. 5,948,666 is hereby withdrawn based on applicants filing of a terminal disclaimer for U.S. Patent No. 5,948,666.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
4/22/2004